d his

(FILE 'HOME' ENTERED AT 16:28:30 ON 24 MAR 2004)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 16:28:52 ON 24 MAR 2004

L1 165 S (NUCLEIC ACID APTAMER)
L2 22 S L1 AND POLYMERASE?
L3 21 DUPLICATE REMOVE L2 (1 DUPLICATE REMOVED)

=>

updated search dates no good.

L/Cook 3/24/04
no PCR

146484-58-4 146484-59-5 146484-61-9 146484-62-0 146484-63-1
146484-64-2 146484-65-3 146484-66-4 146484-67-5 146484-68-6
146484-69-7 146484-70-0 146484-71-1 146484-72-2 146870-92-0D,
derivs. 146870-94-2 149498-54-4 149498-55-5 149498-56-6
149498-57-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin binding and inhibition by)

IT 126320-34-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides contg.)

IT 10043-66-0 10098-91-6 15715-08-9 15750-15-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides labeled with)

IT 14133-76-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides labeled with metastable)

IT 50-99-7, D-Glucose 59-23-4, D-Galactose 617-04-9 1811-31-0
7512-17-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-oligonucleotide complexes dissocn. from immobilized lectin with)

L6 ANSWER 109 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:512963 CAPLUS
DN 119:112963
ED Entered STN: 18 Sep 1993
TI **Aptamers** specific for biomolecules and method of making them
IN Toole, John J.; Griffin, Linda C.; Bock, Louis C.; Latham, John A.; Muenchau, Daryl Dean; Krawczyk, Steven
PA Gilead Sciences, Inc., USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-68
ICS C07H015-12; C07H017-00
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 1, 3
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9214843	A1	19920903	WO 1992-US1383	19920221
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	CA 2104698	AA	19920822	CA 1992-2104698	19920221
	AU 9214354	A1	19920915	AU 1992-14354	19920221
	EP 572529	A1	19931208	EP 1992-907174	19920221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	JP 06508022	T2	19940914	JP 1992-507073	19920221
	US 5582981	A	19961210	US 1994-234613	19940428
	US 5840867	A	19981124	US 1994-237973	19940503

PRAI	US 1991-658796	19910221
	US 1991-658849	19910221
	US 1991-659103	19910221
	US 1991-659113	19910221
	US 1991-659114	19910221
	US 1991-659980	19910221
	US 1991-659981	19910221
	US 1991-744870	19910814
	US 1991-745215	19910814
	US 1991-787921	19911106
	WO 1992-US1383	19920221

AB A method for identifying oligomer sequences which specifically bind target mols. (serum proteins, kinins, eicosanoids, etc.) is described. The technique involves complexation of the target mol. with a mixt. of oligonucleotides contg. random sequences and sequences which serve as **PCR** primers under conditions in which a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixt. The complex is then sepd. from uncomplexed oligonucleotides, and the complexed members of the oligonucleotide mixt. are recovered from the sepd. complex using **PCR**. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, sepn., amplification, and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes. The method is used to generate **aptamers** that bind serum factor X, thrombin, bradykinin, and prostaglandin F2.alpha.. **Aptamer** specificity for binding to and inhibition of thrombin was demonstrated.

ST **aptamer** oligonucleotide prepn; blood coagulation factor X **aptamer**; thrombin **aptamer**; bradykinin **aptamer**; prostaglandin F2 **aptamer**

IT Immunomodulators
(**aptamer** conjugates as)

IT Aflatoxins
Carbohydrates and Sugars, biological studies
Eicosanoids
Peptides, biological studies
Polysaccharides, biological studies
Proteins, biological studies
Steroids, biological studies
Glycerides, biological studies
Glycolipids
Glycoproteins, biological studies
Glycosaminoglycans, biological studies
Lipids, biological studies
Monosaccharides
RL: ANST (Analytical study)
(**aptamer** oligonucleotide binding to)

IT Diagnosis
(**aptamers** for)

IT Deoxyribonucleic acids
RL: ANST (Analytical study)
(**aptamers**, for binding biomols.)

IT Pharmaceuticals
(conjugates, with **aptamers**)

IT Ligands
RL: ANST (Analytical study)
(for cell surface receptors, immunomodulatory conjugates, **aptamers** in relation to)

IT Polymerase chain reaction
Reducing agents
(in **aptamer** prepn.)

IT Receptors
RL: ANST (Analytical study)
(of cell surface, ligands for, immunomodulatory conjugates, **aptamers** in relation to)

IT Immobilization, biochemical
(of target mol., in **aptamer** prepn.)

IT Agglutinins and Lectins
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid support contg., in **aptamer** prepn.)

IT Albumins, biological studies
RL: BIOL (Biological study)
(thrombin **aptamer** binding activity for)

IT Antigens
RL: ANST (Analytical study)
(CD4, **aptamer** oligonucleotide binding to)

IT Glycophosphoproteins
RL: BIOL (Biological study)
(E-selectins, **aptamer** oligonucleotide binding to)

IT Histocompatibility antigens
RL: BIOL (Biological study)
(HLA, **aptamer** oligonucleotide binding to)

IT Glycoproteins, specific or class
RL: BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1), **aptamer** oligonucleotide binding to)

IT Glycoproteins, specific or class
RL: BIOL (Biological study)
(ICAM-2 (intercellular adhesion mol. 2), **aptamer** oligonucleotide binding to)

IT Glycoproteins, specific or class
RL: BIOL (Biological study)
(P-selectins, **aptamer** oligonucleotide binding to)

IT Sialoglycoproteins

RL: ANST (Analytical study)
(VCAM-1 (vascular cell adhesion mol. 1), **aptamer** oligonucleotide binding to)

IT Molecules
(biochem., **aptamer** oligonucleotides binding to)

IT Animal growth regulators
RL: ANST (Analytical study)
(blood platelet-derived growth factors, .alpha.-, **aptamer** oligonucleotide binding to)

IT Animal growth regulators
RL: ANST (Analytical study)
(blood platelet-derived growth factors, .beta.-, **aptamer** oligonucleotide binding to)

IT Antibodies
RL: ANST (Analytical study)
(conjugates, immunomodulatory, **aptamer** in relation to)

IT Radioelements, compounds
Toxins
RL: ANST (Analytical study)
(conjugates, with **aptamers**)

IT Imaging
(contrast agents, conjugates, with **aptamers**)

IT Oligosaccharides
RL: ANST (Analytical study)
(di-, **aptamer** oligonucleotide binding to)

IT Toxins
RL: ANST (Analytical study)
(diphtheria, **aptamer** oligonucleotide binding to)

IT Receptors
RL: ANST (Analytical study)
(epidermal growth factor/.alpha.-transforming growth factor, gene c-erbB, **aptamer** oligonucleotide binding to)

IT Receptors
RL: ANST (Analytical study)
(interleukin 1, **aptamer** oligonucleotide binding to)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 1, receptors, **aptamer** oligonucleotide binding to)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukins, **aptamer** oligonucleotide binding to)

IT Nucleotides, polymers
RL: ANST (Analytical study)
(oligo-, **aptamers**, for binding biomols.)

IT Proteins, specific or class
RL: ANST (Analytical study)
(transforming, **aptamer** oligonucleotide binding to)

IT Receptors
Lymphokines and Cytokines
RL: ANST (Analytical study)
(tumor necrosis factor, **aptamer** oligonucleotide binding to)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(tumor necrosis factor, receptors, **aptamer** oligonucleotide binding to)

IT Animal growth regulators
RL: ANST (Analytical study)
(.alpha.-transforming growth factors, gene c-erbB receptors, **aptamer** oligonucleotide binding to)

IT Gene, animal
RL: ANST (Analytical study)

(c-erbB2, protein product of, **aptamer** oligonucleotide binding to)

IT 9000-94-6, Antithrombin III 9001-12-1, Collagenase 9002-03-3, Dihydrofolate reductase 9004-06-2, Elastase 9027-44-5, Hydroxymethyl glutaryl CoA synthase 62031-54-3, Fibroblast growth factor 107231-12-9, Botulin 51-45-6, Histamine, biological studies
RL: ANST (Analytical study)
(**aptamer** oligonucleotide binding to)

IT 58-82-2, Bradykinin 551-11-1, Prostaglandin F2.alpha. 9001-29-0, Blood-coagulation factor X 9002-04-4, Thrombin
RL: ANST (Analytical study)
(**aptamer** oligonucleotide binding to, prepn. of)

IT 50-99-7, D-Glucose, biological studies 59-23-4, D-Galactose, biological studies 60-24-2, .beta.-Mercaptoethanol 617-04-9, .alpha.-Methyl-mannoside 1811-31-0, N-Acetylgalactosamine 3483-12-3, Dithiothreitol 7512-17-6, N-Acetylglucosamine
RL: ANST (Analytical study)
(in **aptamer** prepn.)

IT 62229-50-9, Epidermal growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor, **aptamer** oligonucleotide binding to)

IT 145563-68-4 145751-88-8 146484-44-8 146484-45-9 146484-46-0 146484-47-1 146484-48-2 146484-49-3 146484-50-6 146484-51-7 146484-52-8 146484-53-9 146484-54-0 146484-55-1 146484-56-2 146484-57-3 146484-58-4 146484-59-5 146484-61-9 146484-62-0 146484-63-1 146484-64-2 146484-65-3 146484-66-4 146484-67-5 146484-68-6 146484-69-7 146484-70-0 146484-71-1 146484-72-2 146484-73-3 149460-11-7
RL: ANST (Analytical study)
(thrombin **aptamer**)

IT 9001-26-7, Prothrombin 9001-90-5, Plasmin
RL: ANST (Analytical study)
(thrombin **aptamer** binding activity for)

IT 77887-18-4
RL: ANST (Analytical study)
(thrombin-binding **aptamer** contg.)

IT 838-07-3, 5-Methyl-2'-deoxycytidine
RL: ANST (Analytical study)
(thrombin-binding **aptamers** contg.)

L6 ANSWER 107 OF 111 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 18
AN 1994:295667 BIOSIS
DN PREV199497308667
TI Isolation and identification of **aptamers** from defibrotide that act as thrombin antagonists in vitro.
AU Bracht, Franzpeter; Schroer, Karsten
CS Institut fuer Pharmakologie, Heinrich-Heine-Universitaet Duesseldorf, D-40225 Duesseldorf, Germany
SO Biochemical and Biophysical Research Communications, (1994) Vol. 200, No. 2, pp. 933-937.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 13 Jul 1994
Last Updated on STN: 24 Aug 1994
AB This study was designed to isolate and identify **aptamer** sequences, acting as thrombin antagonists, from defibrotide, a single-stranded DNA fraction. Two different **aptamers** were identified: 5'GGTTGGATTGGTTGG-3' and 5'-GGTTGGATCGGTTGG-3'. A third **aptamer**: 5'GGATGGATCGGTTGG-3' was found in the **PCR** product from the double-stranded defibrotide precursor. All **aptamers** were potent inhibitors of thrombin-induced platelet aggregation, thromboxane biosynthesis, increase in cytosolic Ca++ and fibrin clot formation, effective concentrations being in the nanomolar range. There was no effect on U 46,619 (thromboxane mimetic) or collagen-induced responses. Similar effects were, obtained with unfractionated defibrotide while the "nonsense" oligonucleotide 5'-GGTGGTGGTTGTGGT-3' was inactive. The data suggest that antithrombin effects of defibrotide are caused by **aptamers**.
CC Cytology - Animal 02506
Genetics - Animal 03506
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Biophysics - Molecular properties and macromolecules 10506
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
In vitro cellular and subcellular studies 32600
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular System (Transport and Circulation); Cell Biology; Genetics
IT Chemicals & Biochemicals
DEFIBROTIDE
IT Miscellaneous Descriptors
ANTIATHEROSCLEROTIC ACTIVITY; ANTITHROMBOTIC ACTIVITY
ORGN Classifier
Mammalia 85700
Super Taxa
Vertebrata; Chordata; Animalia
Organism Name
mammal
Mammalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
RN 83712-60-1 (DEFIBROTIDE)

L6 ANSWER 106 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:291458 CAPLUS
DN 120:291458
ED Entered STN: 11 Jun 1994
TI The use of reversible chemical modification of the backbone of oligonucleotides for **PCR** amplification of **aptamers**
IN Bischofberger, Norbert; Fishback, James A.
PA Gilead Sciences, Inc., USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07H021-00
ICS C07H019-10; C07H019-20; C12Q001-68; A61K031-70
CC 3-1 (Biochemical Genetics)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9404548	A1	19940303	WO 1993-US7130	19930729
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9349948	A1	19940315	AU 1993-49948	19930729
PRAI	US 1992-932189	A	19920819		
	WO 1993-US7130	W	19930729		

AB New **aptamers** with a region capable of specifically binding a target and at least one linking group where P(O)O or P(O)S is replaced by P(O)SR [R = substituted or unsubstituted C1-20 alkyl optionally contg. an ether (-O-) linkage, aryl, alkenyl, cycloalkyl, cycloalkenyl, arylakyl or R1YCOCR3R2 (R1, R2, R3 independently H, C1-9 alkyl; Y = a bond, O, S, NH)] are prepd. The prepn. of these **aptamers** includes treating recovered **aptamers** with base to convert the hydrocarbyl thioate linkages to phosphodiester linkages thereby forming a dehydrocarbylated **aptamer** prior to amplification. The modification is completely reversible allowing selection of the **aptamers** with protected backbones followed by deprotection and amplification of the selected sequences.

ST **aptamer** reversible chem modification backbone selection; oligonucleotide backbone alkylation reversible

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(single-stranded, **aptamers**, reversible chem. modification of backbone in selection of)

IT Nucleotides, polymers
RL: BIOL (Biological study)
(oligo-, **aptamers**, reversible chem. modification of backbone in selection of)

IT Nucleotides, polymers
RL: BIOL (Biological study)
(oligo-, thiophosphate-linked, **aptamers**, reversible chem. modification of backbone in selection of)

IT 135819-94-2 154977-93-2
RL: USES (Uses)
(reversible alkylation of thioate linkage of, reversible modification of backbone in selection of **aptamers** in relation to)

IT 106-95-6, Allyl bromide, reactions 556-56-9, Allyl iodide 620-05-3, Benzyl iodide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reversible alkylation of thioate linkages of oligonucleotides with, reversible modification of backbone in selection of **aptamers** in relation to)

L6 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:114948 CAPLUS
DN 124:167400
ED Entered STN: 23 Feb 1996
TI In vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6
AU Kim, Meehyein; Jeoung, Yeon-Hee; Lee, Seog Jae; Choi, Inpyo; Pyun, Kwang-Ho; Lee, Younghoon
CS Dep. of Chemistry, Korea Advanced Inst. Science and Technology, Taejon, 305-701, S. Korea
SO Molecules and Cells (1995), 5(6), 555-62
CODEN: MOCEEK; ISSN: 1016-8478
PB Korean Society of Molecular Biology
DT Journal
LA English
CC 3-4 (Biochemical Genetics)
AB IL-6 is known to inhibit growth and induce differentiation of several myeloid leukemia cell lines. With the recombinant human interleukin-6 (IL-6) as a target protein, DNA **aptamers** specifically binding to IL-6 were isolated from a random oligodeoxyribonucleotide pool. A large pool of 96-mer oligodeoxyribonucleotides, made up of 60 bases of random sequences flanked by the defined regions of primer binding sites at the 5' and 3' ends, was synthesized. This randomly generated oligodeoxyribonucleotide pool was denatured to generate single-stranded DNA and subjected to in vitro selection with affinity chromatog. and in vitro amplification with polymerase chain reaction (**PCR**) for enrichment in single-stranded DNA **aptamers** specifically binding to IL-6. Multiple rounds of successive affinity chromatog. and **PCR** resulted in the continued purifn. of binding species. The gel retardation expt. showed that **aptamers** had affinity to IL-6 with dissocn. consts. of the order of magnitude of 10-6 M. The sequences of the **aptamers** were identified. A homol. search revealed that they were categorized into at least four groups according to the consensus sequences among them.
ST interleukin 6 DNA binding **aptamer**
IT Deoxyribonucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**aptamer**; in vitro selection of DNA **aptamers** binding to human interleukin-6)
IT Deoxyribonucleic acid sequences
(in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)
IT Lymphokines and Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interleukin 6, in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)

L6 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:392082 CAPLUS
DN 129:38128
ED Entered STN: 26 Jun 1998
TI Thrombin-specific **aptamers** and methods for detection or purification of thrombin
IN Griffin, Linda; Albrecht, Glenn; Latham, John; Leung, Lawrence; Vermaas, Eric; Toole, John J.
PA Gilead Sciences, Inc., USA
SO U.S., 115 pp., Cont. of U. S. Ser. No. 934,387, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12Q001-68
ICS C07K001-14; C07H021-04; C07H021-02
NCL 435006000
CC 7-8 (Enzymes)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5756291	A	19980526	US 1995-484192	19950607
PRAI US 1992-934387		19920821		

AB Methods for detection of thrombin using labeled DNA which specifically binds to thrombin (**aptamers**) and methods for purifn. of thrombin using the unlabeled **aptamers** are disclosed. A method for identifying oligomer sequences, optionally comprising modified bases, which specifically bind target mols. such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate **aptamers** that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface mols. The technique involves complexation of the target mol. with a mixt. of oligonucleotides contg. random sequences and sequences which serve as primer for **PCR** under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixt. The complex is then sepd. from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixt. are recovered from the sepd. complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, sepn., amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary **aptamers**.

ST **aptamer** thrombin detection purifn

IT Selectins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E-; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1); thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(VCAM-1; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT Nucleic acids
Oligonucleotides
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(**aptamers**; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT CD4 (antigen)
Interleukin 1
neu (receptor)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 126320-34-1P 145563-68-4P 146484-44-8P 146484-45-9P 146484-46-0P
146484-47-1P 146484-73-3P 207997-14-6P 207997-15-7P 208057-35-6P
208057-36-7P 208057-37-8P 208057-38-9P 208057-39-0P 208057-40-3P
208057-41-4P 208057-42-5P 208057-43-6P 208057-44-7P 208057-45-8P
208057-46-9P 208057-47-0P 208057-48-1P 208057-49-2P 208057-50-5P
208197-60-8P 208197-61-9P 208197-62-0P 208197-63-1P 208197-64-2P
208197-65-3P 208197-66-4P 208197-67-5P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(thrombin-binding **aptamer**; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 9002-04-4P, Thrombin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 58-82-2, Bradykinin 9001-29-0, Blood-coagulation factor X 106096-93-9, Basic fibroblast growth factor 123123-44-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; WO 9102750 2000 CAPLUS
(2) Anon; WO 9119813 2000 CAPLUS
(3) Aoki; US 4748156 1988 CAPLUS
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(5) Blackwell; Science 1990, V250, P1149 CAPLUS
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(7) Chittenden; Cell 1991, V65, P1073 CAPLUS
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(22) Oliphant; Mol Cell Biol 1989, V9(7), P2944 CAPLUS
(23) Oliphant; Nucl Acids Res 1988, V16(15), P7673 CAPLUS
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(29) Thiesen; Nucleic Acids Res 1990, V18(11), P3203 CAPLUS
(30) Tuerk; Science 1990, V249, P505 CAPLUS
(31) Ullman; Enzyme-Immunoassay 1988, V5, P105
(32) van Lente; Enzyme-Immunoassay 1988, V6, P135

L6 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:392082 CAPLUS
DN 129:38128
ED Entered STN: 26 Jun 1998
TI Thrombin-specific **aptamers** and methods for detection or purification of thrombin
IN Griffin, Linda; Albrecht, Glenn; Latham, John; Leung, Lawrence; Vermaas, Eric; Toole, John J.
PA Gilead Sciences, Inc., USA
SO U.S., 115 pp., Cont. of U. S. Ser. No. 934,387, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12Q001-68
ICS C07K001-14; C07H021-04; C07H021-02
NCL 435006000
CC 7-8 (Enzymes)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5756291	A	19980526	US 1995-484192	19950607
PRAI US 1992-934387		19920821		

AB Methods for detection of thrombin using labeled DNA which specifically binds to thrombin (**aptamers**) and methods for purifn. of thrombin using the unlabeled **aptamers** are disclosed. A method for identifying oligomer sequences, optionally comprising modified bases, which specifically bind target mols. such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate **aptamers** that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface mols. The technique involves complexation of the target mol. with a mixt. of oligonucleotides contg. random sequences and sequences which serve as primer for **PCR** under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixt. The complex is then sepd. from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixt. are recovered from the sepd. complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, sepn., amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary **aptamers**.

ST **aptamer** thrombin detection purifn
IT Selectins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E-; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)
IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1); thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)
IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(VCAM-1; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)
IT Nucleic acids
Oligonucleotides
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(**aptamers**; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT CD4 (antigen)
Interleukin 1
neu (receptor)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 126320-34-1P 145563-68-4P 146484-44-8P 146484-45-9P 146484-46-0P
146484-47-1P 146484-73-3P 207997-14-6P 207997-15-7P 208057-35-6P
208057-36-7P 208057-37-8P 208057-38-9P 208057-39-0P 208057-40-3P
208057-41-4P 208057-42-5P 208057-43-6P 208057-44-7P 208057-45-8P
208057-46-9P 208057-47-0P 208057-48-1P 208057-49-2P 208057-50-5P
208197-60-8P 208197-61-9P 208197-62-0P 208197-63-1P 208197-64-2P
208197-65-3P 208197-66-4P 208197-67-5P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(thrombin-binding **aptamer**; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 9002-04-4P, Thrombin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 58-82-2, Bradykinin 9001-29-0, Blood-coagulation factor X 106096-93-9, Basic fibroblast growth factor 123123-44-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(20) Lindner; Circulation Research 1991, V68, P106 CAPLUS
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(28) Straunton; Cell 1990, V61, P243
(29) Thiesen; Nucleic Acids Res 1990, V18(11), P3203 CAPLUS
(30) Tuerk; Science 1990, V249, P505 CAPLUS
(31) Ullman; Enzyme-Immunoassay 1988, V5, P105
(32) van Lente; Enzyme-Immunoassay 1988, V6, P135

L6 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:114948 CAPLUS
DN 124:167400
ED Entered STN: 23 Feb 1996
TI In vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6
AU Kim, Meehyein; Jeoung, Yeon-Hee; Lee, Seog Jae; Choi, Inpyo; Pyun, Kwang-Ho; Lee, Younghoon
CS Dep. of Chemistry, Korea Advanced Inst. Science and Technology, Taejon, 305-701, S. Korea
SO Molecules and Cells (1995), 5(6), 555-62
CODEN: MOCEEK; ISSN: 1016-8478
PB Korean Society of Molecular Biology
DT Journal
LA English
CC 3-4 (Biochemical Genetics)
AB IL-6 is known to inhibit growth and induce differentiation of several myeloid leukemia cell lines. With the recombinant human interleukin-6 (IL-6) as a target protein, DNA **aptamers** specifically binding to IL-6 were isolated from a random oligodeoxyribonucleotide pool. A large pool of 96-mer oligodeoxyribonucleotides, made up of 60 bases of random sequences flanked by the defined regions of primer binding sites at the 5' and 3' ends, was synthesized. This randomly generated oligodeoxyribonucleotide pool was denatured to generate single-stranded DNA and subjected to in vitro selection with affinity chromatog. and in vitro amplification with polymerase chain reaction (**PCR**) for enrichment in single-stranded DNA **aptamers** specifically binding to IL-6. Multiple rounds of successive affinity chromatog. and **PCR** resulted in the continued purifn. of binding species. The gel retardation expt. showed that **aptamers** had affinity to IL-6 with dissocn. consts. of the order of magnitude of 10-6 M. The sequences of the **aptamers** were identified. A homol. search revealed that they were categorized into at least four groups according to the consensus sequences among them.
ST interleukin 6 DNA binding **aptamer**
IT Deoxyribonucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**aptamer**; in vitro selection of DNA **aptamers** binding to human interleukin-6)
IT Deoxyribonucleic acid sequences
(in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)
IT Lymphokines and Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interleukin 6, in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)

L6 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:392082 CAPLUS
DN 129:38128
ED Entered STN: 26 Jun 1998
TI Thrombin-specific **aptamers** and methods for detection or purification of thrombin
IN Griffin, Linda; Albrecht, Glenn; Latham, John; Leung, Lawrence; Vermaas, Eric; Toole, John J.
PA Gilead Sciences, Inc., USA
SO U.S., 115 pp., Cont. of U. S. Ser. No. 934,387, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12Q001-68
ICS C07K001-14; C07H021-04; C07H021-02
NCL 435006000
CC 7-8 (Enzymes)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5756291	A	19980526	US 1995-484192	19950607
PRAI US 1992-934387		19920821		

AB Methods for detection of thrombin using labeled DNA which specifically binds to thrombin (**aptamers**) and methods for purifn. of thrombin using the unlabeled **aptamers** are disclosed. A method for identifying oligomer sequences, optionally comprising modified bases, which specifically bind target mols. such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate **aptamers** that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface mols. The technique involves complexation of the target mol. with a mixt. of oligonucleotides contg. random sequences and sequences which serve as primer for **PCR** under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixt. The complex is then sepd. from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixt. are recovered from the sepd. complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, sepn., amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary **aptamers**.
ST **aptamer** thrombin detection purifn
IT Selectins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E-; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)
IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1); thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)
IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(VCAM-1; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)
IT Nucleic acids
Oligonucleotides
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(28) Straunton; Cell 1990, V61, P243
(29) Thiesen; Nucleic Acids Res 1990, V18(11), P3203 CAPLUS
(30) Tuerk; Science 1990, V249, P505 CAPLUS
(31) Ullman; Enzyme-Immunoassay 1988, V5, P105
(32) van Lente; Enzyme-Immunoassay 1988, V6, P135

L6 ANSWER 110 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:164224 CAPLUS
DN 118:164224
ED Entered STN: 01 May 1993
TI **Aptamers** specific for thrombin and methods of use
IN Toole, John J.; Griffin, Linda C.; Bock, Louis C.; Latham, John A.; Krawczyk, Steven
PA Gilead Sciences, Inc., USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-68
ICS C07H015-12; C07H017-00
CC 7-3 (Enzymes)
Section cross-reference(s): 1, 3, 9, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9214842	A1	19920903	WO 1992-US1367	19920221
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	CA 2104698	AA	19920822	CA 1992-2104698	19920221
	AU 9214560	A1	19920915	AU 1992-14560	19920221
	US 5582981	A	19961210	US 1994-234613	19940428
	US 5840867	A	19981124	US 1994-237973	19940503
PRAI	US 1991-658849		19910221		
	US 1991-659981		19910221		
	US 1991-744870		19910814		
	US 1991-745215		19910814		
	US 1991-787921		19911106		
	WO 1992-US1367		19920221		

AB Single-stranded thrombin **aptamers** (oligonucleotides that bind specifically to thrombin) are obtained that inhibit both its catalytic activity and its platelet-aggregating activity. The **aptamers**, which show little or no immunogenicity, may be used in treatment or prophylaxis of vascular diseases, inflammatory responses, cancer-related hypercoagulable states, etc., as well as for in vitro or in vivo imaging, diagnosis, thrombin detection and purifn., blood storage, and coating of implant devices. The oligomers are identified by complexation of support-bound thrombin with a mixt. of oligonucleotides contg. random sequences under conditions wherein a complex is formed with the specifically binding sequences but not with other members of the mixt. The thrombin-oligonucleotide complexes are then sepd. from the support and the uncomplexed oligonucleotides, the complexes are dissocd., and the **aptamers** are amplified by std. techniques. The **aptamers** may contain modified bases, sugars, or sugar linkages. Thus, deoxyoligonucleotides were synthesized which contained a random 60-mer sequence between 2 specific 18-mer sequences. The oligomers were heat denatured and applied to a column of thrombin bound to Con A-agarose, and bound oligomers were eluted with buffer contg. thrombin and amplified by **PCR** using the 5' 18-mer and the complement to the 3' 18-mer as primers and the random 96-mer as template. Active clones bound thrombin in the presence of the fibrinogen substrate and contained a consensus sequence, GGNTGGNzGGNTGG (z = 2-5) or a close variant thereof, responsible for thrombin affinity.
ST thrombin oligonucleotide binding
IT Drug delivery systems
(**aptamer** conjugates, thrombin-binding and -inhibiting)
IT Albumins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(binding of, by oligonucleotides)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(immobilized, complexes with thrombin, in prepn. of thrombin-binding and -inhibiting oligonucleotides)

IT DNA
Oligodeoxyribonucleotides, polymers
RNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin binding and inhibition by)

IT Anticoagulants
(thrombin-binding and -inhibiting oligonucleotides)

IT Radionuclides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides labeled with)

IT Monosaccharides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-oligonucleotide complexes dissocn. from immobilized lectin with)

IT Ligands
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(conjugated, with thrombin-binding and -inhibiting oligonucleotides)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(conjugates, with thrombin-binding and -inhibiting oligonucleotides)

IT Imaging agents
(contrast, thrombin-binding and -inhibiting oligonucleotides labeled with)

IT Artery, disease
(coronary, restenosis, treatment of, with thrombin-binding and -inhibiting oligonucleotides)

IT Structure-activity relationship
(thrombin-inhibiting, of oligonucleotides)

IT 9002-04-4, Thrombin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(binding and inhibition of, by oligonucleotides)

IT 9001-26-7, Blood-coagulation factor II 9001-90-5, Plasmin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(binding of, by oligonucleotides)

IT 9002-04-4D, Thrombin, lectin complexes 9012-36-6D, Agarose, Con A conjugates, complexes with thrombin 11028-71-0D, Concanavalin A, thrombin complexes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in thrombin-binding and -inhibiting oligonucleotides prepn.)

IT 554-01-8 77887-18-4 84558-94-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oligonucleotides contg., thrombin binding and inhibition by)

IT 145563-68-4 146484-44-8 146484-45-9 146484-46-0 146484-47-1
146484-48-2 146484-49-3 146484-50-6 146484-51-7 146484-52-8
146484-53-9 146484-54-0 146484-55-1 146484-56-2 146484-57-3